Corcil.

contacting the nucleic acid with at least one type of nanoparticles according to any one of Claims 243[-265] or 253 under conditions effective to allow hybridization of at least one of the types of recognition oligonucleotides on the nanoparticles with the nucleic acid; and

observing a detectable change brought about by hybridization of the recognition oligonucleotides with the nucleic acid.

291. (Amended) A method of detecting a nucleic acid having at least two portions comprising:

providing a type of nanoparticles according to any one of Claims 243[-252] or 253 having recognition oligonucleotides attached thereto, the recognition oligonucleotides on each nanoparticle comprising a sequence complementary to the sequence of at least two portions of the nucleic acid;

contacting the nucleic acid and the nanoparticles under conditions effective to allow hybridization of the oligonucleotides on the nanoparticles with the two or more portions of the nucleic acid; and

observing a detectable change brought about by hybridization of the oligonucleotides on the nanoparticles with the nucleic acid.

292. (Amended) A method of detecting nucleic acid having at least two portions comprising:

contacting the nucleic acid with at least two types of nanoparticles according to [any one of Claims 243-250] Claim 243 having recognition oligonucleotides attached thereto, the recognition oligonucleotides on the first type of nanoparticles comprising a sequence complementary to a first portion of the sequence of the nucleic acid, the recognition oligonucleotides on the second type of nanoparticles comprising a sequence complementary to a second portion of the sequence of the nucleic acid, the contacting taking place under conditions effective to allow hybridization of the recognition oligonucleotides on the nanoparticles with the nucleic acid; and

observing a detectable change brought about by hybridization of the recognition oligonucleotides on the nanoparticles with the nucleic acid.

314. (Amended) A method of detecting a nucleic acid having at least two portions comprising:

providing a type of nanoparticles according to [any one of Claims 253-265] <u>Claim</u> 253 having recognition oligonucleotides attached thereto, the recognition oligonucleotides on each nanoparticle comprising a sequence complementary to the sequence of at least two portions of the nucleic acid;

contacting the nucleic acid and the nanoparticles under conditions effective to allow hybridization of the recognition oligonucleotides on the nanoparticles with the two or more portions of the nucleic acid; and

observing a detectable change brought about by hybridization of the recognition oligonucleotides on the nanoparticles with the nucleic acid.

315. (Amended) A method of detecting nucleic acid having at least two portions comprising:

contacting the nucleic acid with at least two types of nanoparticles according to [any one of Claims 253-263] Claim 253 having recognition oligonucleotides attached thereto, the recognition oligonucleotides on the first type of nanoparticles comprising a sequence complementary to a first portion of the sequence of the nucleic acid, the recognition oligonucleotides on the second type of nanoparticles comprising a sequence complementary to a second portion of the sequence of the nucleic acid, the contacting taking place under conditions effective to allow hybridization of the recognition oligonucleotides on the nanoparticles with the nucleic acid; and

.::

observing a detectable change brought about by hybridization of the recognition oligonucleotides on the nanoparticles with the nucleic acid.

- 360. (Amended) A method of detecting a nucleic acid having at least two portions comprising:
- (a) contacting the nucleic acid with a substrate having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to a first portion of the sequence of said nucleic acid, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the substrate with said nucleic acid;

- (b) contacting said nucleic acid bound to the substrate with a first type of nanoparticles according to [any one of Claims 243-250] Claim 243 having one or more types of recognition oligonucleotides attached thereto, at least one of the types of recognition oligonucleotides comprising a sequence complementary to a second portion of the sequence of said nucleic acid, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the nanoparticles with said nucleic acid; and
 - (c) observing a detectable change.

361. (Amended) The method of Claim 360 further comprising:

- (d) contacting the first type of nanoparticles bound to the substrate with a second type of nanoparticles according to [any one of Claims 243-250] Claim 243 having recognition oligonucleotides attached thereto, at least one of the types of recognition oligonucleotides on the second type of nanoparticles comprising a sequence complementary to the sequence of one of the types of oligonucleotides on the first type of nanoparticles, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the first and second types of nanoparticles; and
 - (e) observing the detectable change.

364. (Amended) The method of Claim 360 further comprising:

- (d) providing a type of binding oligonucleotides having a sequence comprising at least two portions, the first portion being complementary to at least one of the types of oligonucleotides on the first type of nanoparticles;
- (e) contacting the binding oligonucleotides with the first type of nanoparticles bound to the substrate, the contacting taking place under conditions effective to allow hybridization of the binding oligonucleotides with the oligonucleotides on the first type of nanoparticles;
- (f) providing a second type of nanoparticles according to [any one of Claims 243-250] Claim 243 having recognition oligonucleotides attached thereto, at least one of the types of recognition oligonucleotides on the second type of nanoparticles comprising a sequence complementary to the second portion of the sequence of the binding oligonucleotides;

- (g) contacting the binding oligonucleotides bound to the substrate with the second type of nanoparticles, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the second type of nanoparticles with the binding oligonucleotides; and
 - (h) observing the detectable change.
- 384. (Amended) A method of detecting a nucleic acid having at least two portions comprising:
- (a) contacting the nucleic acid with a substrate having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to a first portion of the sequence of said nucleic acid, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the substrate with said nucleic acid;
- (b) contacting said nucleic acid bound to the substrate with a first type of nanoparticles according to [any one of Claims 253-263] Claim 253 having one or more types of recognition oligonucleotides attached thereto, at least one of the types of recognition oligonucleotides comprising a sequence complementary to a second portion of the sequence of said nucleic acid, the contacting taking place under conditions effective to allow hybridization of the recognition oligonucleotides on the nanoparticles with said nucleic acid; and
 - (c) observing a detectable change.
 - 385. (Amended) The method of Claim 384 further comprising:
- (d) contacting the first type of nanoparticles bound to the substrate with a second type of nanoparticles according to [any one of Claims 253-263] Claim 253 having recognition oligonucleotides attached thereto, at least one of the types of recognition oligonucleotides on the second type of nanoparticles comprising a sequence complementary to the sequence of one of the types of oligonucleotides on the first type of nanoparticles, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the first and second types of nanoparticles; and
 - (e) observing the detectable change.
 - 388. (Amended) The method of Claim 384 further comprising:

- (d) providing a type of binding oligonucleotides having a sequence comprising at least two portions, the first portion being complementary to at least one of the types of oligonucleotides on the first type of nanoparticles;
- (e) contacting the binding oligonucleotides with the first type of nanoparticles bound to the substrate, the contacting taking place under conditions effective to allow hybridization of the binding oligonucleotides with the oligonucleotides on the first type of nanoparticles;
- (f) providing a second type of nanoparticles according to [any one of Claims 253-263] Claim 253 having recognition oligonucleotides attached thereto, at least one of the types of recognition oligonucleotides on the second type of nanoparticles comprising a sequence complementary to the second portion of the sequence of the binding oligonucleotides;
- (g) contacting the binding oligonucleotides bound to the substrate with the second type of nanoparticles, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the second type of nanoparticles with the binding oligonucleotides; and
 - (h) observing the detectable change.
- 422. (Amended) A kit comprising a container holding nanoparticles according to any one of Claims 243[-265] or 253.
 - 426. (Amended) A method of nanofabrication comprising

providing at least one type of linking oligonucleotide having a selected sequence, the sequence of each type of linking oligonucleotide having at least two portions;

providing one or more types of nanoparticles according to any one of Claims 243[-265] or 253, the recognition oligonucleotides on each of the types of nanoparticles comprising a sequence complementary to the sequence of a portion of a linking oligonucleotide; and

contacting the linking oligonucleotides and nanoparticles under conditions effective to allow hybridization of the oligonucleotides on the nanoparticles to the linking oligonucleotides so that a desired nanomaterial or nanostructure is formed wherein the nanoparticles are held together by oligonucleotide connectors.

428. (Amended) A method of nanofabrication comprising:

providing at least two types of nanoparticles according to any one of Claims 243[265] or 253,

the recognition oligonucleotides on the first type of nanoparticles comprising a sequence complementary to that of the oligonucleotides on the second of the nanoparticles;

the recognition oligonucleotides on the second type of nanoparticles comprising a sequence complementary to that of the oligonucleotides on the first type of nanoparticles; and contacting the first and second types of nanoparticles under conditions effective to allow hybridization of the oligonucleotides on the nanoparticles to each other so that a desired nanomaterial or nanostructure is formed.

- 430. (Amended) Nanomaterials or nanostructures composed of nanoparticles according to any one of Claims 243[-265] or 253, the nanoparticles being held together by oligonucleotide connectors.
- 432. (Amended) A method of separating a selected nucleic acid having at least two portions from other nucleic acids, the method comprising:

providing two or more types of nanoparticles according to any one of Claims 243[-265] or 253, the oligonucleotides on each of the types of nanoparticles having a sequence complementary to the sequence of one of the portions of the selected nucleic acid; and

contacting the nucleic acids and nanoparticles under conditions effective to allow hybridization of the oligonucleotides on the nanoparticles with the selected nucleic acid so that the nanoparticles hybridized to the selected nucleic acid aggregate and precipitate.

-- 433. The nanoparticles according to any one of claims 243 or 253, wherein the oligonucleotides are attached to the nanoparticles in a stepwise ageing process comprising (i) contacting the oligonucleotides with the nanoparticles in a first aqueous solution for a period of time sufficient to allow some of the oligonucleotides to bind to the nanoparticles; (ii) adding at least one salt to the aqueous solution to create a second aqueous solution; and (iii) contacting the

oligonucleotides and nanoparticles in the second aqueous solution for an additional period of time to enable additional oligonucleotides to bind to the nanoparticles.

- 434. The nanoparticles according to claim 433, wherein the salt solution has an ionic strength sufficient to overcome at least partially the electrostatic attraction or repulsion of the oligonucleotides for the nanoparticles and the electrostatic repulsion of the oligonucleotides for each other.
- 435. The nanoparticles of Claim 433 wherein the nanoparticles are metal nanoparticles or semiconductor nanoparticles.
 - 436. The nanoparticles of Claim 435 wherein the nanoparticles are gold nanoparticles.
- 437. The nanoparticles of Claim 436 wherein the oligonucleotides include a moiety comprising a functional group which can bind to a nanoparticle.
- 438. The nanoparticles of Claim 433 wherein all of the salt is added to the water in a single addition.
 - 439. The nanoparticles of Claim 433 wherein the salt is added gradually over time.
- 440. The nanoparticles of Claim 433 wherein the salt is selected from the group consisting of sodium chloride, magnesium chloride, potassium chloride, ammonium chloride, sodium acetate, ammonium acetate, a combination of two or more of these salts, one of these salts in a phosphate buffer, and a combination of two or more these salts in a phosphate buffer.
- 441. The nanoparticles of Claim 440 wherein the salt is sodium chloride in a phosphate buffer.
- 442. The nanoparticles of Claim 433 wherein the oligonucleotides present on surface of the nanoparticles at a surface density of at least 10 picomoles/cm².

- 443. The nanoparticles of Claim 442 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of at least 15 picomoles/cm².
- 444. The nanoparticles of Claim 443 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of from about 15 picomoles/cm² to about 40 picomoles/cm². -